Generation of HIV-1 Resistant and Functional Macrophages From Hematopoietic Stem Cell-derived Induced Pluripotent Stem Cells.

Journal: Mol Ther

Publication Year: 2011

Authors: Amal Kambal, Gaela Mitchell, Whitney Cary, William Gruenloh, Yunjoon Jung, Stefanos Kalomoiris, Catherine Nacey, Jeannine McGee, Matt Lindsey, Brian Fury, Gerhard Bauer, Jan A Nolta, Joseph S Anderson

PubMed link: 21119622

Funding Grants: Sustained siRNA production from human MSC to treat Huntingtons Disease and other neurodegenerative disorders

Public Summary:
The studies described in this manuscript demonstrate the ability of induced pluripotent stem cells (iPSCs) to develop into cells of the immune system. genes were introduced into the iPSCs that made them resistant to HIV virus infection. The creation of these HIV-1 resistant immune cells highlights the potential use of iPSCs for HIV gene and cellular therapies. Although this work was not directly supported by CIRM, one of the normal donor iPSC lines created in our laboratory for this work (through philanthropic donor funding) was used in Dr. Nolta's CIRM-funded project as a non-affected control for the ongoing Huntington's disease work. The acknowledgements for this manuscript thus state: J.A.N. is supported by the NIH and by the California Institute for Regenerative Medicine.

Scientific Abstract:
Induced pluripotent stem cells (iPSCs) have radically advanced the field of regenerative medicine by making possible the production of patient-specific pluripotent stem cells from adult individuals. By developing iPSCs to treat HIV, there is the potential for generating a continuous supply of therapeutic cells for transplantation into HIV-infected patients. In this study, we have used human hematopoietic stem cells (HSCs) to generate anti-HIV gene expressing iPSCs for HIV gene therapy. HSCs were dedifferentiated into continuously growing iPSC lines with four reprogramming factors and a combination anti-HIV lentiviral vector containing a CCR5 short hairpin RNA (shRNA) and a human/rhesus chimeric TRIM5alpha gene. Upon directed differentiation of the anti-HIV iPSCs toward the hematopoietic lineage, a robust quantity of colony-forming CD133(+) HSCs were obtained. These cells were further differentiated into functional end-stage macrophages which displayed a normal phenotypic profile. Upon viral challenge, the anti-HIV iPSC-derived macrophages exhibited strong protection from HIV-1 infection. Here, we demonstrate the ability of iPSCs to develop into HIV-1 resistant immune cells and highlight the potential use of iPSCs for HIV gene and cellular therapies.